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PRINCIPAL INVESTIGATOR: Darrell Lis, M.S.N.

CONTRACTING ORGANIZATION: Precision Therapeutics, Inc
Pittsburgh, PA 15203

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13. SUPPLEMENTARY NOTES

14. ABSTRACT-The PT-304 study was prematurely terminated on October 1, 2012 primarily due to Precision receiving non-coverage forIn Vitro Chemosensitivity & Chemoresistance Asssays from Medicare. Additionally, our attempts to increase patient accrual throughout the duration of the study were unmet and ultimately the lack of subject recruitment negatively impacted the success of this study.

A total of three-hundred-eighty-five (385) specimens were received by Precision accounting for both pre-treatment and post-treatment samples. Of the specimens received one-hundred-eighty-three (183) were terminated and one-hundred-twelve (112) were screen failures, the remaining two-hundred-two (202) specimens had drug assays completed of which the success rate following quality control was sixty percent. Three-hundred-twenty-seven (327) subjects were enrolled in the trial of which only one-hundred-thirty-four (134) were deemed evaluable. Upon notifying sites of the termination all active subjects were discontinued from participation.

A total of thirty Principal Investigators were approved by the DoD to participate in this study, six investigator sites were prematurely closed prior to the termination of the study notification sent on October 1, 2012. Eleven additional sites have been officially closed with IRBs following the termination of the project and the remaining thirteen sites are in in the process of closing. All sites are expected to be officially closed by the end of the calendar year with the Department of Defense.

15. SUBJECT TERMS- ChemoFX Chemoresponse Assay, Breast Cancer, Prediction of Response

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Introduction

The objective of this study is to develop a biomarker to predict pathological complete response in women treated with neoadjuvant chemotherapy for breast cancer. Such a biomarker would assist physicians in selecting the most effective chemotherapy for the individual patient. The anticipated biomarker will take into account clinical factors (such as tumor stage, tumor size, and age), phenotypic characteristics of the tumor (determined by pathological immunohistochemistry and *ex vivo* chemoresponse assay), and genotypic characteristics of the tumor and patient (determined by genomic profiling via gene expression analysis of tumor RNA). It is expected that collective consideration of all of these factors will be more predictive of patient response to therapy than any of them alone.

Approximately 224 evaluable subjects will be recruited from approximately 20 – 30 US sites. Women with measurable operable invasive breast cancer diagnosed by core needle biopsy will be eligible for this study. Additional tumor specimens will be obtained prior to the start of chemotherapy via core needle biopsies to be used for the *ex vivo* chemoresponse assay and tumor genomic analysis (gene expression), respectively.

All subjects will receive neoadjuvant chemotherapy with one of two standard of care regimens that must consist of the following agents: doxorubicin (A), cyclophosphamide (C), and a taxane (T) such as docetaxel, paclitaxel, or Abraxane (nanoparticle albumin-bound paclitaxel [nab-paclitaxel]); or, docetaxel (T) and cyclophosphamide (C). These must be administered per NCCN guidelines by the treating physician.

Upon completion of chemotherapy treatment, women will undergo lumpectomy, modified radical mastectomy or other surgical procedure determined appropriate by the investigator and at that time will be evaluated for pathological response. At the time of lumpectomy, modified radical mastectomy, or other surgical procedure, additional tumor excess may be sent to Precision Therapeutics, Inc. (Precision) for exploratory analysis if there is no pathologic complete response (pCR), if there are sufficient tumor cells to send, and if the subject agrees to have her excess tumor cells sent to Precision for this purpose.

During the subject's course of participation on the study, the treating physician will remain blinded to the results of the chemoresponse assay and genomic analysis. If it is determined there is no pCR at the time of lumpectomy, modified radical mastectomy or other surgical procedure, or if the subject's condition deteriorates while on chemotherapy and she needs to stop treatment, upon request, Precision will make available a subsequent report to the physician containing additional information about chemotherapy drugs other than ACT that may benefit future treatment decisions for the patient.

Overall Progress

Excluding post-surgical specimens, three hundred thirty five (335) specimens have been received by Precision as of October 1, 2012. Three hundred twenty seven (327) subjects were enrolled in the trial. There are no safety issues (anticipated or unanticipated) to report.

The study was prematurely terminated on October 1, 2012. A total of thirty (30) Principal Investigators were approved by the DoD to participate in this study and six have prematurely closed. On October 1, 2012 all active sites were notified of the decision to terminate the study. Eleven sites have submitted and received IRB acknowledgement of the study closing. The

remaining thirteen sites are in the process of closing. All sites are expected to be closed by the end of the calendar year with the Department of Defense.

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Detailed progress made between September 1, 2012 – report date.

I. Work effort to complete study close out procedures is ongoing with thirteen (13) Investigator sites and is detailed in the table below *(sites highlighted in grey are closed).* Of note the US Oncology sites fall under Study Investigator (SI), Dr. Michael Danso accounting for a total of ten (10) sites, one (1) site previously closed due to the inability to recruit potential subjects.

Participating Sites	**Status Update**
Richard Fine, MD **Advanced Breast Care** 790 Church Street, Suite 410 Marietta, GA 30060	• Closed on June 21, 2012. This investigator relocated practice to another state.
Judy Tjoe, MD **Aurora Health Care Inc.** 8000 Montana Milwaukee, WI 53219	• Notified of study termination on Oct 1, 2012. Activity Sept 2012 • Screened 0 • Enrolled 0
Susan Boolbol, MD **Beth Israel Hospital** 10 Union Square East, Suite 4E New York, NY 10003	• Closed on Oct. 17, 2012 • Activity Sept 2012 • Screened 1 • Enrolled 0
Beth DuPree, MD **Bott Cancer Center at the Holy Redeemer Hospital** 1648 Huntingdon Pike Meadowbrook, PA 19046	• Closed on Oct. 23, 2012 • Activity Sept 2012 • Screened 0 • Enrolled 0
Mark Gittleman, MD **Breast Care Specialists, PC** 250 Cetronia Road, Suite 302 Allentown, PA 18104	• Closed on Oct 9, 2012 • Activity Sept 2012 • Screened 0 • Enrolled 0
Michael Berry, MD **Breast Clinic of Memphis** 1385 West Brierbrook Road Germantown, TN 38138	• Closed on Oct 16, 2012 • Activity Sept 2012 • Screened 0 • Enrolled 0
Theodore Potruch, MD **BreastCare** 2020 Goldring Ave., Suite 206 Las Vegas, NV 89106	• Closed on Oct 3, 2012 • Activity Sept 2012 • Screened 2 • Enrolled 0
John West, MD **BreastLink** 230 South Main Street, Suite 100 Orange, CA 92868	• Closed on Oct 9, 2012 • Activity Sept 2012 • Screened 0 • Enrolled 0

Peter Beitsch, MD
Cancer Solutions
7777 Forest Lane, Suite C-760
Dallas, TX 75320
	• Closed on Oct 4, 2012
	• Activity Sept 2012
	  • Screened 0
	  • Enrolled 0

Walton Taylor, MD
Leading Edge Research, P.A.
9229 LBJ Freeway
Dallas, TX 75243
	• Notified of study termination on Oct 1, 2012
	• Activity Sept 2012
	  • Screened 3
	  • Enrolled 0

Phillip Ley, MD **Mississippi Breast Center** 1030 Flowood Drive, Suite C Flowood, MS 39232	• Closed April 25, 2012.
Aaron Chevinsky, MD **Morristown Memorial Hospital (aka AtlanticHealth)** 95 Madison Avenue, Ste 304c Morristown, NJ 07960	• Closed on September 16, 2011 due to inactivity and non-responsiveness.

Pat Whitworth, MD
Nashville Breast Center, P.C.
300 20th Avenue North, Suite 401
Nashville, TN 37203
	• Closed on Oct 11, 2012
	• Activity Sept 2012
	  • Screened 4
	  • Enrolled 0

James Mackey, MD and Robin Skrine, MD **Southlake Oncology** 1545 E. Southlake Boulevard, Suite 280 Southlake, TX 76092	• Closed on September 14, 2011 due to staffing and logistical issues.

Laura Lawson, MD
St. Thomas Research Institute
4230 Harding Road
Nashville, TN 37205
	• Closed on November 12, 2012
	• Activity Sept 2012
	  • Screened 0
	  • Enrolled 0

Adam Brufsky, MD **University of Pittsburgh Medical Center / University of Pittsburgh Cancer Institute / Magee Women's Hospital of UPMC** 300 Halket Street Pittsburgh, PA 15213-3180	• Closed May 23, 2012 at sponsor request due to lack of interest and no subjects were consented.

William Dooley, MD
University of Oklahoma Health Sciences Center
1000 Stanton L. Young Blvd., LIB 121
Oklahoma City, OK 73117
	• Closure with the local IRB on Oct 27, 2012
	• Activity Sept 2012
	  • Screened 0
	  • Enrolled 0

Agustin Garcia, MD
University of Southern California / Norris Comprehensive Cancer Center
1441 Eastlake Avenue
Los Angeles, CA 90033
	• Notified of study termination on Oct 1, 2012
	• Activity Sept 2012
	  • Screened 0
	  • Enrolled 0

Michael Danso, MD **US Oncology Network** Virginia Oncology Associates 5900 Lake Wright Dr Norfolk, VA 23502	• USOncology IRB notified of study closure next IRB meeting is December 2012 at that time all remaining sites (Allison, Anderson, Caton, Danso, Holmes, McIntyre, Muscato, Osborne, Richards, and Wang) will be officially closed. • Dr. Wilks site closed February 15, 2012 due to lack of subjects for recruitment. • Activity July/Aug 2012 Screened 0 Enrolled 0

Ekaterini Tsiapali, MD
Women and Infants Hospital of RI
101 Dudley Street
Providence, RI 02905
	• Closed on Oct 9, 2012
	• Activity Sept 2012
	  • Screened 0
	  • Enrolled 0

Problem Areas

I. Enrollment

Despite multiple best efforts by DOD and PTI to both extend the time allowed for completion of this study, and many attempts to increase patient accrual; lack of enrollment was the primary issue hindering the successful completion of this project/study. PTI openly discussed this problem with the DOD and both parties decided the project was not salvageable and mutually agreed to terminate the study.

Work to be performed in Next Quarter

Submit the remaining active sites to the Department of Defense for early termination. Provide each site with a PDF copy of the case report forms entered electronically for each subject. Return unused Department of Defense funds supporting this project.

Key Research Accomplishments

Not applicable

Reportable Outcomes

Not applicable

Conclusion

Not applicable

References

Not applicable

Supporting Data

Not applicable

ATTACHMENT 1

Anticipated Accrual from Q2 2011 through Q4 2012

Quarter	Evaluable Enrolled YTD	Target Accrual
Q2 2011	66	70
Q3 2011	82	94
Q4 2011	97	115
Q1 2012	117	149
Q2 2012	128	179
Q3 2012	131	207